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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/769,579	01/25/2001	Hector F. DeLuca	960296.95700	4517

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EXAMINER	
SHAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	16

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/769,579	DELUCA ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Peri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachm nt(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Amendment filed on April 15, 2003 has been entered. Claims 1-5 are pending. Any rejection that is not discussed in this Office Action is considered obviated in view of the Amendment. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

2. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of reducing the risk of the onset of Type I diabetes in the patients with auto antibodies towards glutamic acid decarboxylase or insulin, does not reasonably provide enablement for methods of eliminating the onset or absolutely preventing such diabetes in any human patients.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In particular, the specifications fails to enable the skilled artisan to practice the invention without undue experimentation.

Applicants' arguments with respect to this rejection have been fully considered but are not found persuasive. Applicant argues that the instant specification supports eliminating the onset of Type I diabetes in patients specifically because page 14, line 1-2 of the specification describes eliminating the onset of type I diabetes in 75-90 percent of subjects (see Response at page 6-7). Specifically Applicant argues that the specification demonstrates more than a reduction in the symptoms. *Id.*

In response Examiner first states that the scope of the pending claims are not directed to eliminating the onset of Type I diabetes in 75-90% of predisposed subjects (NOD mouse) by orally administring an effective dose of vitamin D. Rather, the scope is directed to eliminating the onset of Type I diabetes in all human patients. Therefore, Applicants' arguments are not commensurate with the scope of the pending claims.

Second, the fact that only 75-90% of predisposed mice have responded to the treatment methodology is evidence to the lack of absolute prevention of Type I diabetes, as an endpoint, in all human subjects. Thus, undue experimentation is warranted to practice the entire scope of the claim.

Third, there are no guidelines currently setting forth how to eliminate the onset of Type I diabetes in general. Applicant has further failed to provide such evidence to show otherwise. Thus, there is no predictability in the art concerning eliminating the onset or preventing such disease among susceptible patients.

At best, the example solely showed an improved risk/benefit reduction among the sample population. Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the entire scope of the presently claimed invention. Any claim amendment that directs the pending claims to methods of reducing the risk of onset for Type I diabetes in predisposed patients by upto 90 percent or methods of reducing the risk of onset for Type I diabetes in patients with auto antibodies towards glutamic acid decarboxylase would be considered favorably.

3. Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is directed to methods of elimination the onset of Type I diabetes in a human patient. However, the first step of the claim recites "identifying a human Type I diabetes patient." Accordingly, the language of the claim is ambiguous and paradoxical. If the patient undergoing the method is already identifying with a Type I diabetes, as required in the first step of the method, then how can the employment of the instantly claimed method eliminate the onset of Type I diabetes? Clarification is requested.

Claim Rejections - 35 USC § 102

4. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Mathieu et al US Patent 5,665,387.

Mathieu teaches methods of treating autoimmune diabetes which is caused by autoimmune destruction of B cells comprising administering tablets of 1,25 (OH)2D3 to a subject within at similar doses as instantly claimed.. (see col 2, lines 1-10; col 10, lines 1-41; claim 4, 12-17). Autoimmune destruction of B cells leads to Type I diabetes. Accordingly, Mathieu anticipates the limitations of the instant claims.

Claim Rejections - 35 USC § 103

5. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathieu et al (Diabetologia, 1994; 37: 552-558) in view of EURODIAB (PTO-892, filed 10/10/01), Mauricio et al (PTO-892, filed 10/10/01) DeWille et al (US 5,817,351; PTO-892, filed 10/10/01) and Facts and Comparison 1999 (pages 11-15).

Applicant's arguments with respect to this rejection have been fully considered but are not found persuasive.

Applicant's arguments with respect to this rejection have been fully considered but are not found persuasive.

Applicant first argues that the cited reference are describe ordinary Vitamin D is noted, but not persuasive, because the term vitamin D generically describes all steroids that exhibit qualitatively the biological activity of cholecalicfeol (see Dictionary of Biochemistry Molecular biology, 2nd ed. 1991, John Willey & Son). Accordingly, 1 α-hydroxyvitamin D is encompassed by such definition of vitamin D and additionally is well recognized in the art as a potent analog of vitamin D (see Jones, Exhibit A of the Amendment filed on February 25, 02, page 974, 1st col, and its reference 41).

In fact, Applicant's assertion that the cited art describe "ordinary vitamin D" is not understood, as all vitamin D within its generic meaning are expected to provide similar clinical benefit. In fact, Muricio explicitly teaches the beneficial use of the instant species with the genus of vitamin D; therefore using vitamin D for delaying the onset of diabetes is well established.

Applicant also argues that Mauricio does not teach successful treatment, rather it only encourages further research. (see Amendment at page 9). Such argument is also not persuasive because it [O]bviousness does not require absolute predictability of success. Indeed, for many inventions that seem quite obvious, there is no absolute predictability of success until the invention is reduced to practice. *In re O'Farrell*, 7 USPQ2d 1673 at 1680-81 (CAFC 1980) (*citing In re Merck & Co .*, 800 F.2d at 1098,

231 USPQ at 380). Accordingly, the fact that Mauricio did not show successful treatment of diabetes, rather encouraged further research, can not obviate the instant rejection, because Mauricio's statement in view of the combined references provides for such motivation in the art to employ 1, 25 D3.

Moreover, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the rejection of claims 1-5 are based on combined teachings of the cited references not the teachings of anyone individual reference.

Mathieu explicitly teaches that using 1, 25 dihydroxy vitamin D_3 prevents autoimmune diabetes in NOD mice (see abstract, entire pages 555-557). Mathieu does not employ oral vit D compound. EURODIAB and Muricio collectively provides the understanding in the art that vitamin D and analogues thereof, including 1, α-hydroxyvitamin D_3, improves the symptoms of autoimmune diseases and diabetes (see EURODIAB, abstract; Mathieu, pp 552-556; Muricio et al pp 64, 1st col, 2nd paragraph). DeWille shows that all vitamin D such as 1 α vitamin D can be prepared and used orally. (see abstract, examples 12-16). Facts substantiates the teachings of DeWille by providing various forms of oral vitamin D formulations, liquid, capsules, tablets, that are conventionally prepared in the art (pages 11-15, see specifically Cholecalciferol® and Rocaltrol ®or Calderol®).

Thus, all elements of the instant claims are met and the rejection is proper for the reasons of record.

New matter rejection

6. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant case, the recitation of "identifying a human Type I diabetes patient, wherein Type I diabetes is detectable in a patient with autoantibodies to B cell antigens," was not disclosed in neither the specification of the instant application or the claims. Accordingly, the claims are rejected as to contain new matter because there is no indication that Applicant had possession of such method step at the application was filed.

Conclusion

No claims are allowed. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on April 15, 2003 and the amendments to the claims prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

SS 11/20/03

RUSSELL TRAVERS
PRIMARY EXAMINER